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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/489,667 | 01/19/2000 | Stephen Donovan | D-2875 | 6119 |

7590 12/12/2001

Frank J Uxa
4 Venture Suite 300
Irvine, CA 92618

[REDACTED] EXAMINER

KAM, CHIH MIN

| ART UNIT | PAPER NUMBER |
|----------|--------------|
| 1653 | [REDACTED] |

DATE MAILED: 12/12/2001

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Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|------------------------|----------------------|---------------------|
| Advisory Action | Applicant No. | Applicant(s) |
| | 09/489,667 | DONOVAN, STEPHEN |
| | Examiner | Art Unit |
| | Chih-Min Kam | 1653 |

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

THE REPLY FILED 21 September 2001 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) The period for reply expires 3 months from the mailing date of the final rejection.
- b) The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. The proposed amendment(s) will not be entered because:
 - (a) they raise new issues that would require further consideration and/or search (see NOTE below);
 - (b) they raise the issue of new matter (see Note below);
 - (c) they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 - (d) they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3. Applicant's reply has overcome the following rejection(s): _____.
4. Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. The a) affidavit, b) exhibit, or c) request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
6. The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. For purposes of Appeal, the proposed amendment(s) a) will not be entered or b) will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: _____.

Claim(s) withdrawn from consideration: _____.

8. The proposed drawing correction filed on _____ is a)a) approved or b)b) disapproved by the Examiner.
9. Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.
10. Other: _____.

Continuation of 2. NOTE: The amendment to the claims does not resolve the current issue under 35 USC 112 first and second paragraphs. The amendment and response of 21 September 2001 also raise additional issues. Claims 79 and 80 have been amended to include a Hc of the botulinum toxin having been modified, which needs to be further searched and re-examined. Applicants' response has been fully considered, however, claims 67 and 68 remain rejected under 35 USC 112 first and second paragraphs, and the rebuttal is shown as follows:

The rebuttal to the applicants' response:

Claims 67 and 68 encompass an agent for treating pain comprising a clostridial neurotoxin component covalently attached to a precursor or an analog of substance P. Applicants argue that the precursors and analogs of substance P can similarly be attached to a clostridial neurotoxin component to reduce pain (page 5, fifth paragraph), it is not necessary to disclose an example of every species covered by a claim (page 4, fourth paragraph). Applicants further assert that U.S. Patent 5,891,842 has disclosed one precursor of substance P (substance P-G) is fully active (page 8, second paragraph), and the unpredictability in the art regarding precursors or analogs of substance P should be provided (page 7, third paragraph). The argument is found not persuasive because the specification indicates the target moieties are "components that are substantially similar to the transmission compounds", and further define the term as "molecules or substances that have the same function as that of the transmission compounds", for example, glutamate agonists, (page 24, lines 17-30), thus, the target moiety in the instant application is substance P or an agonist of substance P, which would have the same function as substance P. However, this is not the case for analogs or precursors of substance P since most substance P compounds are antagonists of substance P, for example, Folkers et al. (U. S. Patent 4,481,139) indicate substance P analogs are potent antagonists (columns 5-7; Table IV); Coy et al. (U. S. Patent 5,410,019) indicate linear peptide analogs of substance P with modification in the peptide bond and amino acid residues can inhibit substance P-stimulated amylase release, but one analog has an agonist activity (columns 13 and 14; Table 3). The precursors and analogs of substance P can similarly be attached to a clostridial neurotoxin component as indicated in the specification, however, the agent containing the precursors and analogs might not have the same effect as substance P. The analog shown in U.S. Patent 5,891,842 is one example which has the same function as substance P, however, analogs or precursors with different sequences do not appear to work in the same manner as substance P as indicated in the examples above. Therefore, it is necessary to carry out further experimentation on the analogs or precursors of substance P as the target moiety to assess the effect of the agent containing the analogs or precursors in treating pain since the analogs or precursors with various structures might not have the same function as substance P. The Folkers and Coy et al. patents are provided here solely in rebuttal of applicants' comments in the response.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8:00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CMK
December 10, 2001

Christopher S. F. Low
CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600